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10/802,273	03/17/2004	Gustavo C. Rodriguez	31162B	4202

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RAYMOND N. NIMROD
623 MILBURN
EVANSTON, IL 60201

EXAMINER	
ROYDS, LESLIE A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,273	RODRIGUEZ, GUSTAVO C.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2007 and 29 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 are presented for examination.

Applicant's Amendment filed April 20, 2007, and the duplicate papers filed May 29, 2007, have each been received and entered into the present application.

Claims 1-24 are pending and under examination. Claims 1, 7-9, 16, 19 and 22-23 are amended and claims 25-26 are cancelled.

Applicant's arguments, filed April 20, 2007 and May 29, 2007, have been fully considered. Rejections and objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons of record set forth at pages 3-5 of the previous Office Action dated October 20, 2006, of which said reasons are herein incorporated by reference.

Applicant traverses the instant rejection, stating that the specification at page 35, line 19-page 36, line 11, describes various mono-phasic or multi-phasic OCP regimens that contain dosages of norgestimate. Applicant further submits, "...while the paragraph specifies the higher dosages of the multi-phasic regimen, it does not explicitly recite the lower dosages in the other phases. Applicant respectfully submits that it would be readily apparent to a person of ordinary skill in the art that the teachings would apply to 'multi-phasic OCP regimens' that contain norgestimate, including those norgestimate dosages in

multi-phasic regimens that are disclosed in the specification...A person skilled in the art would readily understand that where only one dosage is taught for one of the phases, yet the disclosure states that it is useful in 'multi-phasic OCP regimens' containing norgestimate, that would be fully applicable to the norgestimate dosages in tri-phasic regimen disclosed on page 6 for norgestimate." (p.5, Applicant's remarks)

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

Initially, it is noted that the present issue at hand is that Applicant has failed to provide any teaching, either explicit or implicit, in the instant disclosure as originally filed to direct the skilled artisan to employ a multi-phasic hormonal regimen wherein one of the phases is that which Applicant regards as the novel concept of the invention (i.e., at least 0.5 mg norgestimate in combination with 20-35 mcg or at least 20 to less than 35 mcg ethinyl estradiol equivalent) is placed in combination with an additional hormonal regimen phase of the prior art (i.e., a tri-phasic regimen of norgestimate with 0.18, 0.215 or 0.25 mg norgestimate). Though the specification may disclose prior art hormonal regimens, including the tri-phasic regimen of norgestimate with 0.18, 0.215 or 0.25 mg norgestimate, the assertion of a lack of adequate written support is clearly proper because the disclosure conspicuously lacks any implicit, let alone explicit, suggestion to combine Applicant's hormonal regimen with a hormonal regimen of the prior art, particularly the tri-phasic norgestimate regimen of 0.18, 0.215 or 0.25 mg norgestimate.

The fact that such a combination may have been obvious to, or "readily understood", by one of ordinary skill in the art at the time of the invention is insufficient to establish that such a concept was, in fact, in possession of Applicant at the time of the invention. Applicant is arguing a standard of what the skilled artisan would have readily understood, or have taken as an obvious modification, from the disclosure rather than what is specifically disclosed and/or described in the specification in such a way to reasonably convey to the skilled artisan that the instant inventor actually had possession of the invention

as now claimed. In the present case, it remains that the specification lacks any teaching of a combination of the claimed hormonal regimen with a prior art hormonal regimen to render a multi-phasic hormonal regimen as now claimed in instant claims 20-22 and the allegation that a person skilled in the art would have readily understood that, where only one dosage is taught for one of the phases of a "multi-phasic OCP regimen" containing norgestimate, that a tri-phasic *prior art* regimen (such as, e.g., the 0.18 mg, 0.215 mg or 0.25 mg regimen of norgestimate as disclosed at page 6 of the specification) would be included as the second or subsequent phase, is not persuasive in establishing error in the propriety of the rejection.

In view of such, it is clear that the specification clearly lacks written support for the limitations of present claims 20-22 directed to the concept of a multi-phasic hormonal regimen wherein one norgestimate phase is at least 0.5 mg and another phase has a daily dosage of 0.18-0.25 mg, specifically, 0.18 mg or 0.215 mg. Moreover, Applicant has failed to persuasively argue or point to disclosure that is reasonably supportive of the concept of combining the hormonal regimen that Applicant regards as the novel concept of the invention (i.e., at least 0.5 mg norgestimate in combination with 20-35 mcg or at least 20 to less than 35 mcg ethinyl estradiol equivalent) with an additional phase constituting a hormonal regimen of the prior art (i.e., a tri-phasic regimen of norgestimate with 0.18, 0.215 or 0.25 mg norgestimate) in the teachings and disclosure of both the specification and claims as originally filed. Accordingly, the conclusion of a lack of adequate written description for the subject matter of present claims 20-22 remains proper.

For these reasons, and those previously made of record at pages 3-5 of the Office Action dated October 20, 2006, rejection of claims 20-22 remains proper and is **maintained**.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 22 has been amended to now be dependent from claim 23, which is directed to a hormonal regimen comprising daily sequential dosages wherein at least one of the daily dosages comprises at least 0.5 mg of norgestimate and an estrogen component in the range of 20-35 mcg Ethinyl Estradiol (EE) equivalent, wherein said regimen is multi-phasic, with one phase having a daily dosage of norgestimate of at least 0.5 mg and has another phase with a daily dosage of norgestimate of 0.2-0.3 mg.

In particular, it is unclear whether present claim 22 is intended to further limit the "another phase" described in present claim 23 to, specifically, one with a daily dosage of norgestimate of 0.215 mg, or whether it is intended to circumscribe an additional phase other than the "one phase" and "another phase" described in present claim 23. In other words, it is unclear whether claim 22 is intended to define an at least tri-phasic regimen or whether it is intended to further limit the at least bi-phasic regimen of claim 23.

For these reasons, the skilled artisan would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection. In view of the fact that the claim fails to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, the present rejection under 35 U.S.C. 112, second paragraph, is proper.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pasquale (U.S. Patent No. 4,544,554; 1985) in view of Elliesen et al. (WO 97/11680; 1997), each already of record.

Pasquale teaches tri-phasic oral contraceptive regimens comprising an estrogen and a progestogen component (see abstract), provided in a pharmaceutical unit, such as a transparent package having 28 dosage units arranged sequentially and consisting of 7 tablets for the first phase, 7 tablets for the second phase, 7 tablets for the third phase and followed by 7 placebo units, wherein a single tablet is to be taken each day over a period of 28 days (col.3, lines 38-45). Pasquale teaches the estrogen component in a daily dosage amount equivalent to 0.02-0.05 mg (i.e., 20-50 mcg) 17alpha-ethinyl estradiol (col.2, lines 47-54), wherein the preferred estrogen is 17alpha-ethinyl estradiol (col.2, lines 59-6). Pasquale teaches norgestimate (i.e., D-17beta-acetoxy-13beta-ethyl-17alpha-ethinyl-gon-4-en-3-one oxime) as a preferred progestogen component (col.3, lines 10-12).

Please reference the exemplary regimens discussed as Examples 2 and 4 of Pasquale at columns 4-5. Example 2 teaches a tri-phasic regimen comprising a first phase of 0.035 mg 17alpha-ethinylestradiol with 0.50 mg norgestimate; a second phase of 0.035 mg 17alpha-ethinylestradiol with 0.75 mg norgestimate; and a third phase of 0.035 mg 17alpha-ethinylestradiol with 1.0 mg norgestimate. Thus, total norgestimate administered over the entire regimen is equivalent to (0.5 mg/tablet x 7 tablets)+(0.75 mg/tablet x 7 tablets)+(1.0 mg/tablet x 7 tablets) = 0.25+5.25+7=12.5 mg norgestimate (i.e., at least 8 mg norgestimate as required by claims 17 or 24 or at least 12 mg norgestimate as required by claim 18). Example 4 teaches a tri-phasic regimen comprising a first phase of 0.035 mg 17alpha-ethinylestradiol with 0.18 mg norgestimate; a second phase of 0.035 mg 17alpha-ethinylestradiol with 0.215 mg norgestimate; and a third phase of 0.035 mg 17alpha-ethinylestradiol with 0.25 mg norgestimate.

Though the exemplary regimens of Pasquale employ 17alpha-ethinyl estradiol in an amount of 0.035 mg (i.e., 35 mcg), the teachings and disclosure of the reference are not solely limited to that which is exemplified. In fact, Pasquale states at col.3, lines 47-50, "The following preferred specific embodiments are to be construed as merely illustrative of the invention and are not meant to limit the invention in any way." Such a statement is clearly indicative of the fact that other products falling within the scope of the invention disclosed by Pasquale are contemplated and disclosed by the reference, even though they may not have been specifically exemplified. In fact, one of ordinary skill in the art would have understood the exemplified regimens of Pasquale as guidance for preparing other products with varying amounts of estrogen (i.e., 17alpha-ethinyl estradiol) and progestogen (i.e., norgestimate) than those exemplified but within the scope of the teachings, with the reasonable expectation of success that the formulated product would have had the same contraceptive properties. Specifically, Pasquale teaches daily dosages of about 0.02-0.05 mg of 17alpha-ethinyl estradiol (i.e., amounts overlapping those claimed in newly amended claim 1), preferably 0.035 mg (col.2, l.47-54), for use in the context of the disclosed contraceptive regimens, which is clear evidence that contraceptive regimens comprising between 20-50 mcg (i.e., equivalent to 0.02-0.05 mg) 17alpha-ethinyl estradiol were contemplated by Pasquale, despite the fact that the reference exemplifies regimens using the preferred dosage of 35 mcg. Although 35 mcg may be the preferable amount of estrogen, the fact remains that Pasquale clearly discloses that estrogen in the amount of 20-50 mcg may be used substantially interchangeably in the context of the disclosed regimens while preserving the contraceptive properties of the hormonal composition. Accordingly, such disclosure amounts to a clear and unequivocal teaching of the use of 17alpha-ethinyl estradiol in an amount of between 20-50 mcg, which overlaps directly with the amounts of ethinyl estradiol equivalents claimed (i.e., at least 20 to less than 35 mcg as recited in claim 1 or 20-35 mcg as recited in claim 7, 16 and 23).

The differences between the Pasquale reference and the presently claimed subject matter lies in that the reference fails to teach norgestimate in dosages of 0.8 mg (claim 11), greater than 1.0 mg (claims 7-9), or total norgestimate of at least 20 mg (claims 19); or a multi-phasic regimen with another phase having norgestimate in an amount of 0.2-0.3 mg (claims 16 or 23), 0.18-0.25 mg (claim 20), 0.18 mg (claim 21), or 0.215 mg (claim 22).

However the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

Elliesen et al. provides teachings that frequent modifications to the progesterone dosage level are necessary to deal with hormonal fluctuations due to the physiological differences between women. Elliesen et al. states, "Modifying the progesterone dosage level also is frequently necessary during menopause to deal with menses irregularities. Thus, a fixed combination of an estrogen dosage and a progestogen dosage that is suitable for all menopausal women is impossible to design, for a variety of reasons. One reason is the wide variation from individual to individual in the resorption rate which exists with all modes of administration except intravenous, which is not practiced in HRT. These differences in bioavailability can reach 100% or more. For example, the bioavailability of estradiol orally averages 5% of the oral dose, which means that in an individual it can be as low as 3% or as high as 6%. Another reason why a fixed combination is not suitable is because of variations in body weight and fat mass proportion, which has an endocrine function because it contains enzymes to transform hormonal precursors into estrogens. A third reason is the interaction between estrogens and progestogens, i.e., progestogens may only become effective in the presence of estrogens because they stimulate the production of progestogen receptors." (page 2, para.3-4)

In light of such a teaching, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the specific dosage amounts of norgestimate as taught by Pasquale to tailor the regimen to

fit the hormonal requirements of the subject to whom it was administered. In particular, one of skill in the art would have been motivated to augment or increase the dosage of norgestimate to, for example, 0.8 mg (claim 11), greater than 1.0 mg (i.e., 1.2 or 1.8 or 2.5 mg; claims 7-9), or total norgestimate of at least 20 mg (claim 19), depending on the hormonal needs of the female (i.e., time of reproductive cycle, menses, menopause, etc.) and physiological factors (i.e., age, weight, lean muscle/fat mass ratio, etc.). In particular, increasing the progestogen dosage would have naturally commended itself to the skilled artisan in order to maintain an efficacious anti-fertility level of the progestogen hormone when accounting for differing, and possibly slower, rates of hormone resorption and metabolism among individual female subjects.

Applicant is further reminded that should he rely upon the fact that a particular amount of the progestogen agent is critical to the invention, Applicant must make an objective showing that the claimed range achieves unexpected results relative to the prior art range [*In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)] and that the unexpected results demonstrate a marked improvement over that achieved using the amounts of the prior art such that the difference shown is actually a difference in kind and not just a difference in degree [*In re Waymouth*, 499 F.2d 1273, 1276, 182 USPQ 290. 293 (CCPA 1974)]. Furthermore, Applicant is advised that should he rely upon unexpected results to patentably distinguish over the prior art, the present claims must be limited to that embodiment which is, in fact, unexpected.

Regarding the use of an additional phase having norgestimate in an amount of 0.2-0.3 mg (claims 16 or 23), 0.18-0.25 mg (claim 20), 0.18 mg (claim 21), or 0.215 mg (claim 22), Pasquale expressly teaches an exemplary regimen wherein norgestimate is administered concomitantly with 0.035 mg 17alpha-ethinylestradiol in three phases of 0.18 mg norgestimate, 0.215 mg norgestimate and 0.25 mg norgestimate. Pasquale teaches the same contraceptive efficacy of this regimen as compared to the regimen of Example 2 (i.e., norgestimate in an amount of at least 0.5 mg). The skilled artisan would have

been motivated to employ such an alternate phase in the hormonal regimen(s) disclosed by Pasquale because prolonged treatment with excessively high levels of progestogen can lead to hormonal side effects such as, but not limited to, those taught by Elliesen et al. at the top of page 2, including breast tenderness, nausea, edema, menstrual disorders, etc., and, therefore, the use of a multi-phasic regimen wherein the dosage amounts of the progestogen are varied such that the efficacy of the regimen is maintained while avoiding the adverse side effects typically seen with protracted administration of high levels of progestogen(s) would have been *prima facie* obvious to one of ordinary skill in the art.

Response to Applicant's Arguments

Applicant traverses the combination of Pasquale and Elliesen et al., stating that Pasquale deals with OCP (oral contraceptive) formulations having generally higher hormonal dosages than the HRT formulations and Elliesen et al. deals with HRT regimens that can be modified because of issues during menopause, which clearly has nothing to do with OCP formulations as taught by Pasquale.

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

In response thereto, Applicant is restricting consideration of Elliesen et al. solely to the fact that the reference teaches the modification of HRT regimens because of issues during menopause, but fails to address the larger teaching and, thus, suggestion, of Elliesen et al. to modify the dosage amounts of estrogen and progestogen in hormonal formulations, be it oral contraceptive or hormone replacement therapy. Elliesen et al. specifically names factors that affect the need for variable dosage amounts of estrogen and progestogen, such as innate resorption rate, which, in turn, affects the bioavailability of the hormone(s), variations in body weight and fat mass proportion and the natural interactions between estrogens and progestogens (i.e., progestogens may only become effective in the presence of estrogens because they stimulate the production of progestogen receptors), which are clearly factors that would be

considered by the skilled artisan during the process of determining the optimal amounts for a hormonal regimen, regardless of the intended use of the hormonal regimen for contraception or replacement therapy.

In view of such teachings, it is clear that one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to alter the dosage amounts of the estrogen and/or progestogen component of the hormonal regimen depending upon the needs of the individual to be treated. Furthermore, the fact that the art recognized such a need for tailoring hormonal regimens to the specific individual to be treated is a clear recognition that the determination of the optimal dosage amounts was a practice well within the knowledge of the skilled artisan and, thus, did not amount to undue experimentation in order to make such a determination. Accordingly, and further in the absence of any showing, either in the form of evidence or reasoning, that such determination was not within the skill of the artisan and/or that the claimed amounts are critical to the invention (i.e., a showing of unexpected results), it remains that Elliesen et al. supports the conclusion of *prima facie* obviousness with regard to the determination of the optimal dosage amounts for the disclosed hormonal regimen, absent factual evidence to the contrary.

For these reasons, and those presented *supra*, claims 1-24 remain properly rejected under 35 U.S.C. 103(a).

Conclusion

Rejection of claims 1-24 remains proper and is **maintained**.

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie A. Royds
Patent Examiner
Art Unit 1614

August 13, 2007

8/16/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER